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Autistic Characteristics in Adults with Epilepsy

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Abstract:

The reported prevalence of autism spectrum disorders in people with epilepsy ranges from 15%-47% [1-3]. Despite the high co-morbidity, there has been a lack of systematic studies of autistic characteristics in epilepsy. According to Spence and Schneider [4], almost nothing is known about the relationship of epilepsy to the core characteristics of autism. The aim of these experiments is to measure autistic traits and characteristics in adults with epilepsy who do not have a diagnosis of any autism disorder. *Method:* We investigated autistic characteristics in adults with and without epilepsy employing the Autism Spectrum Quotient (epilepsy $n=40$, control $n=38$) [5], and systemizing and empathising abilities employing the Intuitive Physics Test and the Adult Eyes Task-Revised (epilepsy $n=19$, control $n=23$) [6, 7]. *Results:* Significantly more autistic behavioural traits, as measured by the AQ, were related to having epilepsy, but intact systemizing and empathising abilities in these adults suggest that in adults with epilepsy autism-like symptoms may be present in the absence of cognitive profiles characteristic of autism. *Conclusion:* Increased autistic characteristics found in adults with epilepsy without an ASD diagnosis suggests that epilepsy syndromes may incorporate behavioural aspects of autism in the absence of some of its core cognitive features.

Keywords: Epilepsy; Autism; Autistic Traits; Seizures; Autism Spectrum Disorders; Co-morbidity; Asperger Condition; Asperger Disorder; Empathising; Systemizing.

1. Introduction

Epilepsy is a neurological disorder characterised by an enduring predisposition to manifest epileptic seizures, and the definition of epilepsy requires the occurrence of at least one epileptic seizure [8]. Autism spectrum disorder (ASD) is a severe neurodevelopmental disorder, characterised by impairments in social interaction, communication, and by restricted and repetitive activities and interests [9]. Notably, autistic traits are highly heritable and there is strong evidence for ASD as a trait condition [10]. In contrast, epilepsy is often non-heritable and can be acquired, although more recently, Voets and colleagues have suggested that Temporal Lobe Epilepsy (TLE) may be the result of a neuro-developmental disorder [11]. Prevalence rates for ASD in epilepsy range from 15%-47%, and while it is unclear if ASD are under-diagnosed in adults, high rates of under-diagnosis have been found in children [1, 12, 13]. Childhood epilepsy onset is considered to be a significant factor for ASD [14, 15]. Unsurprisingly therefore, ASD may be under-diagnosed in children with epilepsy [1, 3, 12, 13]. Several researchers have suggested that current psychological assessment methods fail to detect autistic characteristics in epilepsy, and Steffenberg suggests that ASD may be overlooked due to lack of sensitive

instruments to assess ASD in epilepsy [12]. Matsuo and colleagues state that it is important to suspect ASD in every patient with epilepsy [3]. Notably, Berg and colleagues have recently proposed mandatory ASD screening in all children with epilepsy [16].

Despite the high co-morbidity, according to Spence and Schneider little is known about the relationship of epilepsy to the core features of autism [4]. Further, Besag highlights that there is a remarkable lack of systematic studies on the behavioural characteristics of childhood epilepsy [17]. A high rate of epileptic discharges (85.8%) have recently been identified in a study examining 1014 individuals with ASD, and earlier research has related these discharges to severity of ASD [18]. During a review of the current use of anti-epileptic drugs [AEDs] for the treatment of ASD, Di Martino and Tuchman found that AEDs were a significant factor for improving deficits in two of the three core characteristics of autism: communication and socialisation, which occurred regardless of seizure control [19]. These improvements suggest that AEDs significantly reduce autistic characteristics and may mask autistic characteristics in a research and clinical environment.

The aim of this study is to investigate behavioural autistic traits in adults with epilepsy, and at the same time to investigate the presence of characteristics in this population that have been proposed to relate to an underlying neurocognitive basis for autism: a deficit in empathising abilities and intact or enhanced systemizing abilities, as proposed by the Empathising-Systemizing [E-S] theory [20]. Research of sex differences in the general population have found that males obtain higher systemizing than empathising scores, and higher systemizing scores than females, while females display the opposite profile. These findings led researchers to investigate adults with ASD, and postulate that they are characterised by a deficit in empathising abilities and intact or enhanced systemizing abilities [20]. A study by Lai and colleagues found similar performance on measures of systemizing ability and measures of empathy between males and females with Asperger Syndrome/high-functioning autism [21]. This suggests that the E-S profile applies to both genders of adults with ASD.

According to Baron-Cohen, systemizing is defined by the drive to analyse or construct a system or variables in a system, and rules or laws that govern the behaviour of a system and enable prediction of how the system will behave [22]. However, there is a lack in research of systemizing abilities in adults with epilepsy, and despite recent evidence of increased autistic traits, it is unknown whether adults with epilepsy focus specifically on systems or have enhanced systemizing abilities.

The word empathy means to experience something from the other person's point of view [23]. Measures of recognition of facial emotion recognition [FER] are a well-accepted index of empathising ability. While individuals with ASD can be impaired detecting basic emotions in the whole face, crucially Loveland and colleagues found that those with ASD were most impaired at recognising mental states from the eyes alone [24]. This led to the development of a tool which tests the ability to discriminate emotions from expressions in the eyes [7, 22]. However, more recent research now suggests that emotional empathy may be intact in some adults with Asperger Syndrome, and additionally some inconsistent findings of a FER deficit in ASD have been reported as well as one comparable performance on the Adult Eyes test between adults with and without AS [25, 26]. Harms and colleagues conclude that when behavioural studies are reviewed as a whole, they are only slightly more likely to find a deficit of FER in ASD than not, and they suggest that some adults with ASD may use compensatory mechanisms [26]. Despite this contradictory finding, the E-S theory is well supported, and has been found to implicate levels of foetal testosterone to the relationship between systemizing and

empathising abilities, and to levels of autistic traits [27]. Further, Wheelwright and colleagues demonstrated that autistic traits in adults can be predicted from measures of empathising and systemizing abilities [28].

There is a growing body of evidence that adults with epilepsy have impairments of FER, and adults with Frontal Lobe Epilepsy are specifically impaired in the ability to perceive emotion from the eyes [29, 30]. Permanent deficits in FER ability found in adults with TLE are considered to be related to early insult and right medial temporal structures [31, 32]. Interestingly, male gender in epilepsy has been related to both of these factors, signifying that males are especially vulnerable to FER impairment [33, 34]. Whilst this research does not aim to explore the E-S theory, investigating empathising and systemizing ability in adults with epilepsy is appropriate for established whether other abilities are intact in adults with epilepsy, and may have some value when investigating autistic traits.

Experiment 1 investigated the extent of autistic traits in epilepsy. It employed the Autism Spectrum Quotient (AQ) which is designed to measure the degree to which an adult with normal intelligence in the general population has autistic traits [5]. It assessed social skills, attention switching, imagination, attention-to-detail, and communication. In individuals with epilepsy, there is some reason to suspect impaired social skills [35-37], poorer communication [38, 39], enhanced attention-to-detail [40] and impaired cognitive flexibility [41]. Investigation of imaginative ability has been lacking, and there is genuine uncertainty about whether all 5 autistic subscales, as considered by the AQ, may be impaired. However based on the overall evidence, it is hypothesised that there will more autistic traits in adults with epilepsy than without.

Experiment 2 aimed to be the first study to measure systemizing abilities in adults with epilepsy, by employing the Intuitive Physics Test (IP). Research has shown that this ability can be retained or enhanced in those with more autistic traits and ASD, therefore the aim of this experiment was to assess whether adults with epilepsy have a wider pattern of autism-related cognitive features, in addition to the clinical features assessed by the AQ. In the absence of evidence of systemizing abilities in epilepsy, it is hypothesised that there will be no difference between groups in systemizing ability.

As described above, several studies of social cognition in people with epilepsy have reported deficits in facial emotion recognition. Therefore Experiment 3 employed the Adult Eyes Task-Revised, which was originally developed to test emotion recognition and empathising ability in people with autism [7]. Based on previous evidence, it is predicted that an impairment will be demonstrated.

Hypotheses

Experiment 1. *H1*: adults with epilepsy will demonstrate increased autistic traits compared to adults without epilepsy;

Experiment 2. *H2*: there will be no difference in systemizing ability between adults with and without epilepsy;

Experiment 3. *H3*: adults with epilepsy will demonstrate impaired empathising abilities compared to adults without epilepsy.

2. Method

These experiments recruited two groups of adults: a control group without epilepsy, and a heterogeneous group with epilepsy (*see tables below*).

Experiment 1

Participants

Method of Recruitment

This experiment mainly used an event sampling method, and included Epilepsy charity conferences and University of Bath [UoB] home webpage adverts. Participants without epilepsy were recruited from students at the UoB, or were known to the epilepsy participants, eg. an unrelated friend or partner.

Exclusion criteria

Participants with epilepsy were excluded if they had a diagnosis of an ASD, or did not meet the criteria for active epilepsy. Active epilepsy taken from the Engel Class, was defined as one or more seizure in the preceding 12 months with or without AED discontinuation, and is a conservative adaption of Engel IC. Participants without epilepsy were excluded if they had a diagnosis of an ASD, or any seizure disorder. Only adults (≥ 18 years) participated. No participant throughout this research had an autism-epilepsy syndrome, eg. Dravet's Syndrome. Participants self-reported their epilepsy type. No respondents with epilepsy were excluded for inactive seizure activity or an ASD.

Participant Samples

Respondents were participants who completed some or all of their personal details, along with the AQ on the surveymonkey website. Total respondents with epilepsy: $n=77$, total participants who failed to complete the AQ: $n=37$, with only $n=40$ of these completed the task, revealing a high dropout rate during the task of 48%. The sample comprised $n=78$: Control Group $n=38$, Epilepsy $n=40$, (*see Tables 1 and 2*).

Missing Data

The data revealed that all participants with epilepsy who omitted 3 or more responses failed to complete the questionnaire. The omission of 3 or more responses occurred at the early stages of completing the AQ, within the first 10 questions. If ≥ 3 responses were left blank, their response was considered incomplete and the participants' data was excluded. By comparison, this is less than other studies employing the AQ. For example, Hoekstra and colleagues used 5 omitted responses (10%, for one condition) for an exclusion threshold [42].

However, the epilepsy group have severe difficulties which may impact on their ability to undertake an assessment requiring 50 responses. There were no participants with epilepsy who completed the AQ but omitted more than 2 responses. Therefore the exclusion threshold was set at ≥ 3 omitted responses, which resulted in failure to complete the questionnaire. Participants with epilepsy who failed to complete the AQ ($n=37$). Missing data values (<3 omitted responses) were replaced by the median value for each item.

Table 1: Demographics

	Controls $n=38$			Epilepsy $n=40$		
	Female $n=27$, Male $n=11$			Female $n=25$; Male $n=15$		
	Mean	SD	Range	Mean	SD	Range
Age	42.1	(13.2)	22.4-70.9	40.6	(14.7)	19.3-71.2

Table 2: Classification of epilepsy type

Primary Type of Epilepsy	Epilepsy	%
Temporal Lobe Epilepsy	12	30.0
Other Focal Epilepsy	5	12.5
Absence Epilepsy	5	12.5
Myoclonic Epilepsy	3	7.5
Idiopathic Generalised Epilepsy	4	10.0
Unknown	11	27.5
Total	40	100.0

Epilepsy classification was self-reported by participants, primary epilepsy type at diagnosis was used for classification of epilepsy type.

Onset of Epilepsy

Participants with epilepsy self-reported their epilepsy onset as: childhood-onset epilepsy $n=8$, adulthood onset epilepsy $n=24$, and unknown, $n=18$.

Experiments 2 and 3

Participants

Method of Recruitment

This sample was recruited predominantly from the sample for Experiment 1 [$n=42$; epilepsy $n=19$, control $n=23$]. Additional participants were recruited from: Epilepsy charity conferences, UoB website, and adverts through University Psychology Departments. Participants without epilepsy were recruited from students at UoB.

Exclusion criteria

Exclusion criteria was the same as Experiment 1. Three participants with epilepsy were excluded: one had prior knowledge of the tests, one did not correctly follow the instructions, and one participant did not return the Adult Eyes Task-Revised. Participants from Experiment 1 were re-checked to ensure that they met the criteria for ‘active epilepsy’ defined in Experiment 1 when they participated later in Experiments 2 and 3.

Participant Sample

The sample comprised $n=42$ adults: Control Group $n=23$, and Epilepsy Group $n=19$, (*see Tables 3 and 4*).

Table 3: Demographics

	Controls $n=23$			Epilepsy $n=19$		
	Female $n=17$, Male $n=6$			Female $n=13$, Male $n=6$		
	<i>Mean</i>	<i>SD</i>	<i>Range</i>	<i>Mean</i>	<i>SD</i>	<i>Range</i>
Age	55.7	(26.8)	22.6-66.5	36.2	(11.2)	18.4-56.1

Table 4: Classification of epilepsy type

Primary Type of Epilepsy	<i>n</i>	<i>%</i>
Temporal Lobe Epilepsy	6	31.5
Frontal Lobe Epilepsy	2	10.5
Complex Partial Epilepsy	3	15.8
Juvenile Myoclonic Epilepsy	1	5.3
Other Focal Epilepsy	1	5.3
Myoclonic Epilepsy	1	5.3
Tonic-Clonic Epilepsy	5	26.3
Total	19	100.0

Epilepsy classification was self-reported by participants, primary epilepsy type at diagnosis was used for classification of epilepsy type.

2.1 Psychological assessment

Experiment 1

The Autism Spectrum Quotient (AQ) was provided in paper format and digital format. Participants were provided with: i) personal details form, ii) AQ and instructions or AQ (epilepsy-specific) and instructions, iii) and a feedback form.

The Autism Spectrum Quotient

The AQ is a structured questionnaire developed to assess autistic traits in adults with normal intelligence [5]. It has good screening properties at a threshold score of 26 [5, 43]. Participants self-rated their responses on a 4-point Likert Scale, and each statement scores 0 or 1. The total range of scores was 0 to 50.

Design

The experiment was conducted as an independent-samples design. The independent variable was group: Epilepsy or no Epilepsy. The dependent variable was score.

Experiments 2 & 3

Participants were provided with: i) personal details form, ii) a paper-based version of the Intuitive Physics Test and the Adult Eyes Task-Revised, and standard instructions; iii) a feedback form.

The Intuitive Physics Test

This test was developed to assess the perception of physical causality and higher-level understanding of physical-causality, that is, understanding the mechanical reasoning of how things work with respect to the properties of physical objects [6]. The test items are images of mechanisms, with related questions about what will happen next. The example provided in the instructions to participants depicts an angled beam and various arrows which indicate pivot points underneath, which would balance the beam. In total, the test comprises of 20 questions with a multiple choice format with 4 options, only one response is correct. The total range of scores was 0 to 20. Time for the duration of the test was self-reported (minutes and seconds).

The Adult Eyes Task-Revised

The Adult Eyes Task-Revised was developed from The Reading the 'Mind in the Eyes' Task, to assess the ability to correctly recognise facial expressions of emotion from the eyes [7]. The task presents a series of photographs of the eyes region of faces. The stimuli comprised of black/white photographs of male/female actors, only their eyes are presented, without other facial features such as the mouth. There are 36 presentations, one per A4 sheet, size 115mm x 45mm. There are 4 response options (forced-choice words) distributed at each corner of the stimuli. The practice example depicts a photograph of eyes, and offers 4 potential responses: *jealous, panicked, arrogant, or hateful*. Only one response is correct. The total range of scores was 0 to 36.

Missing Data

There were no missing data.

Design

This experiment was conducted as an independent-samples design. The independent variable was group: Epilepsy or no Epilepsy. The dependent variable was score.

2.2 Procedure

Experiment 1

Participants were invited to take part in a study investigating cognition and behaviour in adults with and without epilepsy. Participants were provided with a paper copy of the AQ, and invited to self-rate themselves by

responding to the statements designed to identify traits. Participants were invited to complete the AQ in their own time.

Experiments 2 and 3

Participants who responded to the advert for Experiment 1 were invited by email afterwards to take part in a second study investigating cognition and behaviour. Respondents were posted the materials with standard instructions to record their time for the IP test.

Response rates

Response rates from both groups of participants were low, however epilepsy participants were especially low: Control participants: 23 of 32 completed responses [71.9%]; Epilepsy participants: 19 of 63 completed responses [30.2%].

Ethical considerations

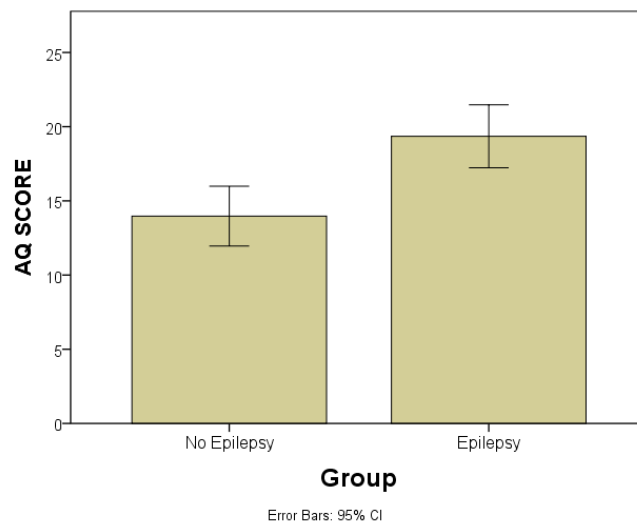
The research was approved by the UoB Department Of Psychology Ethics Committee.

3. Results

Experiment 1

Analysis was conducted for group differences on AQ score. Negatively skewed data was corrected by square root transformation. An independent t-test showed a significant difference between adults with epilepsy and adults without epilepsy ($t=-3.71$, $df=76$, $p<.001$), see Figure 5. This revealed a large effect size (Cohen's $d=0.841$).

Figure 5: *AQ Score by Group*



Experiment 2

Intuitive Physics test

Analysis explored group differences between adults with and without epilepsy for score. Kolmogorov test confirmed normal distribution ($p>.05$), while Levene's test revealed a lack of homogeneity ($p>.045$). An independent t-test on 'score' revealed that there was no significant group difference when equal variances were not assumed ($t=.254$, $df=41$, $p=0.80$, *n.s.*). An independent t-test on 'time' for positively skewed data which was corrected by square root transformation revealed no significant group difference ($t=-.421$, $df=41$, $p=0.676$, *n.s.*), see Table 6.

Experiment 3

Adult Eyes Task-Revised

Analysis explored group differences for score. Negatively skewed data was corrected by square root transformation. An independent t-test on 'score' revealed that there was no significant group difference ($t=.188$, $df=41$, $p=0.85$, *n.s.*), see Table 6.

Table 6: *Intuitive Physics and Adult-Eyes Task-Revised, mean scores and time*

	Controls (<i>n</i>=23)	Epilepsy (<i>n</i>=19)
	<i>Mean (SD)</i>	<i>Mean (SD)</i>
Adult-Eyes, Score	27.22 (SD=3.15)	26.79 (SD=4.98)
Intuitive Physics Score	10.39 (SD=2.52)	11.16 (SD=3.29)
Intuitive Physics Time (secs.)	10.50 (SD=4.59)	11.00 (SD=4.44)

No further exploration was undertaken.

4. Discussion

Experiment 1 explored autistic traits in adults with epilepsy without any autism disorder. It was predicted that adults with epilepsy would demonstrate increased autistic traits compared to adults without epilepsy. Consistent with this hypothesis (H1), a significant increase in autistic traits was found. The AQ demonstrates good screening properties at a threshold score of 26 [43]. Threshold scores of 26 and above were found for 16% [$n=5$] of adults with epilepsy. This might suggest that around a sixth of adults with epilepsy but no diagnosis of ASD have autistic traits at a level that can be indicative of an ASD diagnosis. This may also be an under-estimate,

however, as 95% of adults with epilepsy in the present study were taking AEDs, which significantly reduce autistic characteristics [19]. Experiments 2 and 3 explored performance on the IP test and the Adult Eyes Task-Revised as measures of empathising and systemizing abilities in adults with and without epilepsy. It was predicted that there would be no group difference in systemizing abilities, and that adults with epilepsy would demonstrate decreased empathising abilities. As predicted, the results from Experiment 2 showed no difference between systemizing ability between adults with and without epilepsy, therefore the null hypothesis H2 was accepted. Contrary to what was predicted, the results from Experiment 3 showed no decrease in empathising abilities in adults with epilepsy compared to adults without epilepsy. Therefore the experimental hypothesis H3 was rejected. This is contrary to previous studies which have demonstrated an impairment of FER in some epilepsy types [29-34].

Various papers have pointed out relatively high comorbidities between the diagnosis of epilepsy and the diagnosis of autism. The comorbidity rates are reported to be higher in those with $IQ < 70$. However in this study, whilst IQ was not measured, the study methods are likely to have ruled out the participation of those with a significant intellectual disability. Although this comorbidity has been well reported, a detailed examination of how different features of autism co-exist in people with epilepsy has not yet been clearly defined, and the relationship of the core features are not yet understood.

The profile of which aspects of autistic symptomatology are over-represented in those with epilepsy compared to those without epilepsy may contribute to the understanding of the basis of the apparent comorbidity. Therefore in this study, the levels of the behavioural symptoms of autism in people with epilepsy, as described using the AQ, were examined along with an investigation of whether specific cognitive profiles seen in autism, (enhanced systemizing abilities and decreased empathising abilities measured by a task of facial emotion recognition from photographs of the eyes) were also present.

It was observed that while the autism-like behaviours measured by the AQ were increased in those with epilepsy compared to those without epilepsy, there were no increases in specific cognitive processes that have been widely reported in autism, characterised by enhanced systemizing and decreased empathising ability. This suggests, at least in those with epilepsy in the absence of a significant intellectual disability, that the increased rates of autism symptomatology that have been reported are not necessarily the result of the co-existence of a diagnosis of autism as it occurs in those without epilepsy, but rather that they could be the manifestation of a partial phenocopy of the condition. If this observation is confirmed in other studies, it suggests that part of the syndrome of epilepsy may include symptoms that resemble some aspects of autism, but with a different aetiology, towards which future research could be directed.

4.1 Limitations

There were several limitations of these experiments. AEDs have been found to be a significant factor for improving deficits in two of the three core characteristics of autism: communication and socialisation, which may mask autistic characteristics in a research environment. Despite this, evidence has demonstrated impairments of FER in adults with some epilepsy types. In addition, the effects on performance of individual

differences in AED usage were unknown. Although the AQ was developed to measure adults with normal intelligence and the intelligence quotient of the sample was unknown, the study methods are likely to have ruled out the participation of those with an intellectual disability. Statements about childhood in the AQ may not be appropriate for adults with adulthood-onset of epilepsy. This research was limited by poor participant response for Experiments 2 and 3, and a lack of male participants with epilepsy.

5. Conclusion

Previous studies have highlighted the high co-morbidity between epilepsy and autism, however a detailed examination of how different features of autism co-exist in people with epilepsy has not been clearly defined. These experiments investigated autistic characteristics in a heterogeneous group of adults with epilepsy without an ASD diagnosis. The findings suggest that in addition to the high co-morbidity of autism found in people with epilepsy, adults with epilepsy without a diagnosed autism disorder have more autistic behavioural traits, without any increase in the specific cognitive processes found in autism. None of the participants had been diagnosed with any ASD, and therefore these increased characteristics may have previously been unrecognised in these adults. The findings suggest that epilepsy syndromes may incorporate behavioural aspects of autism in the absence of some of its core cognitive features.

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